

Epidemiology of emerging foodborne pathogens

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Abstract

Foodborne diseases still represent an important global public health issue, including Europe and Italy, which endangers the health of the population and leads to socio-economic costs and a threat to the market trend. In developed countries it is estimated that up to one third of the population are affected by microbiological foodborne diseases each year. In these countries, it has been observed that traditional infectious foodborne diseases have decreased while re-emerging and emerging pathogens like *Escherichia coli* O157, *Listeria monocytogenes*, *Campylobacter jejuni*, *Norovirus* and Hepatitis A virus have increased.

In 2004, in Italy the incidence for Listeriosis was 0.06 per 100,000 population and is included among the statutory notifiable diseases.

E. coli O157:H7 is not subject to statutory notification in Italy; however, a voluntary national surveillance system for HUS in paediatric patients and for VTEC, has led to the notification of 429 paediatric HUS cases and 344 clinical cases of VTEC from 1988 to 2004. Data on campylobacteriosis are available thanks to the voluntary notifications received from the Enternet Laboratories: 582 cases were isolated from human clinical specimens in 2004. Furthermore, data from a specific surveillance system for acute viral hepatitis (SEIEVA) shows that the incidence of reported cases in Italy is declining.

The necessity to alert the authorities responsible for epidemiological surveillance nationally remains paramount. Communication as well as educational campaigns aimed at different target groups, for example consumers, will play an important role in the prevention of foodborne diseases.

Key words: foodborne diseases, emerging pathogens, re-emerging pathogens

Introduction

Social, environmental, economic and technological challenges facing food demand, production and distribution have increased the risk of epizootic, zoonotic and food-related diseases. The increased average age of the population, urbanization, emigration, mass tourism and the globalisation of the food market have led to major food habit changes; hence, the rise in the diffusion of foodborne diseases sustained by classic and emerging pathogens. Simultaneously, there has been a growing demand for healthier, high-quality food sustainability and safer agricultural, farming, aquaculture and fishery production.

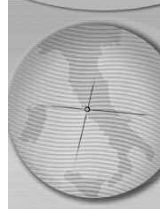
20th-century advances such as pasteurisation and refrigeration, and more recent improvements in hazard analysis and control along the production chain, have contributed to ameliorate the microbiological safety of most foods. Nevertheless, at the start of the 21st century, foodborne diseases remain a significant cause of morbidity and mortality both in the developed and, above all, in the developing world. It is estimated that each year foodborne diseases cause

approximately 76 million illnesses, 325,000 hospitalisations, 5,000 deaths in the USA and 2,366,000 cases, 21,138 hospitalisations, 718 deaths in England and Wales [1, 2].

In developed countries it is estimated that up to one third of the population are affected by microbiological foodborne diseases each year [3]. In these countries, it has been observed that traditional infectious foodborne diseases have decreased while re-emerging and emerging pathogens like *Escherichia coli* O157, *Listeria monocytogenes*, *Campylobacter jejuni*, *Norovirus* and Hepatitis A virus have increased [4].

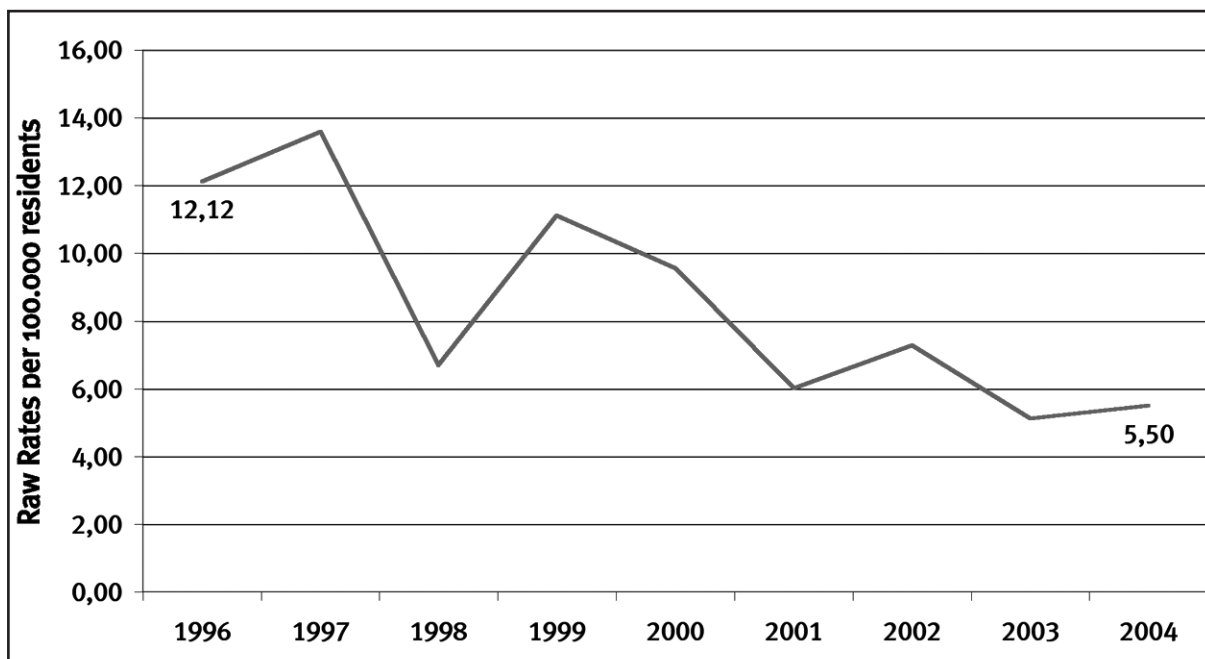
In Italy, from 1993 to 2004, the incidence of foodborne diseases decreased significantly (Figure 1). Contrarily and of epidemiological interest, is the increased incidence of diarrhoeal infections. (Figure 2) [5, 6]. These data suggest the inefficacy of preventive action in reducing the incidence of infectious diarrhoea related to emerging pathogens.

The trend in infectious diarrhea could be correlated to emerging pathogens (*Campylobacter* spp., *E. coli* O157, *Listeria monocytogenes*) that are not yet included in large epidemiological



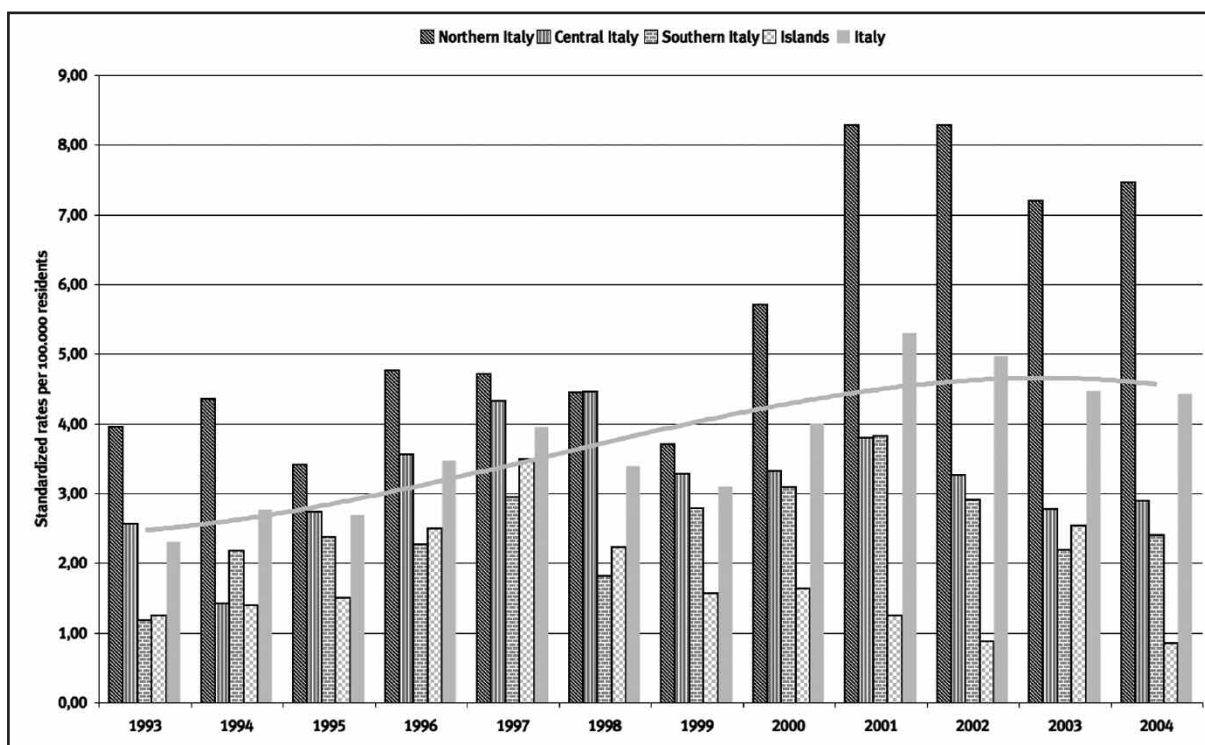
ITALIAN JOURNAL OF PUBLIC HEALTH

Figure 1. Incidence of foodborne diseases in Italy (raw rates per 100,000 residents), from 1996 to 2004.



Source: Bollettino Epidemiologico del Ministero della Salute [Epidemiology Bulletin of the Ministry of Health] [29]; ISTAT. Health for All. Italy, 2005.

Figure 2 – Incidence of diarrhoeal infections in Italy (standardised rates by age per 100,000 residents), from 1993 to 2004.



Source: Bollettino Epidemiologico del Ministero della Salute [Epidemiology Bulletin of the Ministry of Health] [29].

surveillance programmes.

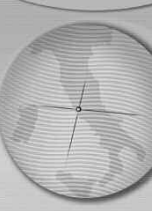
This paper will briefly describe the epidemiology of the most important emerging foodborne pathogens involved in foodborne diseases:

- Bacteria (*E.coli* O157; *Listeria monocytogenes*, *Campylobacter* spp.)

- Viruses (Noroviruses; Hepatitis A virus).

Emerging foodborne bacteria

Diarrhoeal diseases due to emerging pathogenic bacteria seem to have increased significantly over recent years. The authors briefly describe three of



the most important emerging foodborne zoonotic pathogens: *Escherichia coli* O157, *Listeria monocytogenes*, *Campylobacter* spp.

Escherichia coli is a common inhabitant of the gut of humans and warm-blooded animals. Most strains of *E. coli* are harmless but a minority are potentially pathogenic for humans including serotype O157, which in humans is capable of causing severe foodborne diseases, such as hemorrhagic colitis and hemolytic uremic syndrome (HUS) [7].

E. coli O157 belongs to the group of enterohaemorrhagic *E. coli* (EHEC) that produce one or more bacteriophage-encoded Shiga-like toxins, also called verocitotoxins (VT1, VT2), which are characterized by their capability of intimately adhering to the intestinal mucosa by an attaching and effacing mechanism [8, 9].

Among the verocitotoxin-producing *E. coli* (VTEC), the serotype primarily involved in infections seems to be O157; however, in recent years, other O-serotypes of *E. coli*, such as O26, O103, O111, O118 and O145, have become of increasingly important epidemiological value both in Europe and in Italy [10].

The reservoir for VTEC appears to be principally the gastro-intestinal systems of cattle and other ruminants [11].

Humans are infected with VTEC primarily through the consumption of contaminated foods, such as raw or undercooked ground meat products (undercooked hamburgers, dried, cured salami), untreated milk and milk products (yoghurt, cheese), fruit (unpasteurized fresh-pressed apple cider) and vegetables (sprouts, lettuce, coleslaw and salad).

Person-to-person contact is an important mode of transmission, and occurs through the oral-faecal route [12].

Faecal contamination of water and other foods, as well as cross-contamination during food preparation (originating from beef and other meat products, contaminated surfaces and kitchen utensils), can also cause infection [7, 13-15].

Escherichia coli O157 is capable of surviving the rigorous processing steps during the manufacturing of dry fermented sausages. While the addition of probiotic organisms generally inhibits *E. coli* O157:H7 during dry fermented sausage manufacturing processes, microencapsulation of probiotic organisms has proved to reduce their inhibitory action against *Escherichia coli* O157:H7 [16].

In the EU, where diagnostic practices vary between countries and regions thus making direct comparisons difficult, trends in the incidences

can still be compared and seems to be lower than in the USA. During the period 1998-2002, the annual incidence in OECD (Organisation for Economic Cooperation and Development) countries for VTEC, was between 0.03 and 10.4 cases/100,000 inhabitants [17].

In Italy, VTEC and HUS infections are not subject to statutory notification; a national voluntary surveillance system for HUS in paediatric patients and for VTEC, has been in operation since 1988, with a total of 429 paediatric HUS cases from 1988 to 2004 and 344 clinical cases of VTEC [18] being reported. Each year an average of 30 HUS cases in children between 0 and 14 are reported, with an average incidence of around 0.3 cases/100,000 inhabitants, which is relatively low compared with other European countries [17]. The great majority of cases were registered in paediatrics, especially in patients under 5 years of age [17]. During the period 1988-2004, the most frequently isolated serogroup was O157 (39.3% of isolations), followed by serogroup O26 (21.1%) [18].

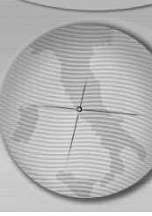
Outbreaks identified through the registration of clusters of HUS cases have been reported in 1992 (nine cases of serotype O111), in 1993 (fifteen cases of serotype O157) and in 1997 (nine cases of serotype O111) [18].

Amongst emerging foodborne pathogens, *Listeria monocytogenes* has become, in recent years, a significant threat to public health, especially for its ubiquitary distribution and its ability to persist in food-processing environments and multiply under refrigeration conditions, which is different from most foodborne pathogens which, at low temperatures enter a phase of inactivity [19].

Several virulence factors of *Listeria monocytogenes* have been identified and extensively characterized at the molecular and cell biologic levels, including the hemolysin (listeriolysin O), two distinct phospholipases, a protein (ActA), several internalins, and others [20].

Certain groups within the general population are particularly susceptible to infection, namely immunocompromised persons, (e.g. organ transplant or cancer patients), HIV-infected individuals, pregnant women, newborn babies and the elderly [21].

Various clinical manifestations are associated with listeriosis and these can be grouped into two categories: invasive listeriosis and non-invasive listeriosis. Invasive listeriosis are cases when initial infections of the intestinal tissue by *L. monocytogenes* lead to invasion of otherwise sterile body sites, such as the pregnant uterus, the central nervous system, or the blood, or



combinations of these [22]. Non-invasive listeriosis (referred to as febrile listerial gastroenteritis) leads to the development of gastroenteritis, such as diarrhoea, fever, headache and myalgia, after a short incubation period [23].

In recent years, antimicrobial resistance of *Listeria* spp has emerged. Studies have shown that several species of *Listeria* isolated from humans or from food production or processing facilities are resistant to one or more antibiotics [24].

Listeria monocytogenes has been isolated in at least 37 species of mammals, both domestic and wild, in 17 bird species as well as in fish and crustaceans [25].

Common-source outbreaks have been associated with or linked epidemiologically with the consumption of soft cheeses; hot dogs; pork tongue in aspic; pate; chocolate milk; milk; butter; smoked mussels; smoked fish; raw salad and coleslaw [26].

Although exposure to the bacterium is common, listeriosis is rare amongst the general population; in 2002, the reported incidence of listeriosis in Europe ranged from 0.3 to 7.5 cases per million inhabitants [27]. The highest rates were reported from countries that had statutory notification for listeria infections and surveillance through a national reference laboratory [28]. The associated mortality rate is between 20 and 30% [22, 2]. *Listeria monocytogenes* infections are responsible for the highest hospitalisation rates (91%) amongst known foodborne pathogens and have been linked to sporadic episodes and large outbreaks of human illness worldwide [19].

In Italy, in 2004, 30 cases were notified [29], with an incidence of 0.06 cases per 100,000 inhabitants. The number of notifications has increased since 1990 [6], when listeriosis was included among statutory notification diseases of Class II [30].

The reported incidence of listeriosis seems to be lower in Italy than in most EU countries and the United States (0.30 cases per 100,000 inhabitants in 2005) [31]. This could reflect both a real lower diffusion of the disease in Italy or a specific issue of undernotification [32].

Campylobacter spp. are one of the three genera of the family Campylobacteriaceae (*Arcobacter*, *Helicobacter* and *Campylobacter*) and includes about 15 species, 3 of which are considered to be pathogenic to humans as they are associated with foodborne diseases: *C. jejuni*, *C. coli* and *C. lari* [33]. The reservoir for this pathogen is the intestine of wild, farm and domestic warm-blooded animals (cattle, pigs, dogs, poultry, birds) [34]. It is more frequently isolated from poultry

and it is transmitted through contaminated water or cross-contamination between raw meat (poultry) and other foods (raw milk, other kinds of meat, vegetables) [35].

Campylobacter is the cause of foodborne infections with an incubation of 3-5 days, but exceptions to this have been recorded and can include an incubation period ranging from 1.5 to 7-10 days. Symptoms can include minor to severe diarrhoea lasting from 2 to 10 days, which can also require 2-5 days of hospitalization. Intestinal (haemorrhage, acute cholecystitis) and extraintestinal (bacteraemia, reactive arthritis, Guillain-Barré syndrome) complications requiring longer periods of hospitalisation are also possible [33].

In many developed as well as developing countries *Campylobacter* is considered to be the main factor in enteric infections. An increase in the diffusion of antibiotic-resistant strains has also been observed among isolates from both humans and animals [36].

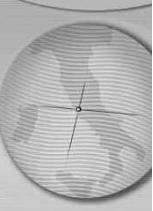
In the USA during 2005, the incidence of *Campylobacter* per 100,000 population was 12.72. The estimated annual *Campylobacter* infection incidence has decreased by 30%, with a significant decline in the incidence from 1996-1998 to 2005 [31].

In 2003, reported notifications in the European Union (13 Member States) and Norway accounted for 135,974 human cases of campylobacteriosis. This confirms the decreasing trend in notifications, which had been observed in 2002, with an overall reduction of 9% [37].

In Italy, data on campylobacteriosis are not available, since it is not included among statutory notification diseases [30]. However, thanks to the voluntary notifications of Enternet Laboratories, 582 *Campylobacter* spp. were isolated from human clinical specimens in Italy in 2004; 80% were *C. jejuni* and 40% of them proved to be ciprofloxacin-resistant. Enternet has also reported an increase in *Campylobacter* spp. notifications in Italy. Consequently, there is a need to alert the authorities responsible for national epidemiological surveillance to this issue [10].

Foodborne Viruses

The importance of foodborne transmission of viruses is becoming increasingly recognized; numerous viruses can be implicated in foodborne and waterborne outbreaks. There are more than 100 known human enteric viruses which are divided into several groups on the basis of morphological, physical, chemical and antigenic differences [38]. However, only a few enteric



viruses have been shown epidemiologically to be transmitted via food or water. Food and waterborne viruses can be divided into three disease categories:

- Viruses that cause gastroenteritis (astrovirus, rotavirus, adenovirus types 40 and 41, and the two genera of enteric caliciviruses, "Noroviruses" (NV) and the typical caliciviruses or "Sapoviruses").
- Faecal-orally transmitted hepatitis viruses: Hepatitis A virus (HAV) and Hepatitis E virus.
- Viruses which cause other illnesses, e.g. enteroviruses [39].

Different to bacterial contamination, viral contamination of food does not increase during processing, and it may actually decrease. Most food or waterborne viruses are relatively resistant to heat, disinfection and pH changes. It is not a coincidence that most virus groups implicated in outbreaks are small, non-enveloped particles, rather than large, fragile, enveloped viruses [39] with a low infection dose of perhaps 10-100 virus particles.

The enteric viruses most commonly transmitted by food are NV and HAV. HAV infection will result in non-specific symptoms like fever, headache, fatigue, nausea and vomiting, followed by signs of hepatitis 1-2 weeks later. Viral shedding typically continues until 1 week after onset of jaundice in adults and 1-2 weeks in children, although prolonged intermittent shedding may occur for up to 90 days in patients with clinical relapses. Relapses have been reported in 1.5 to 18.5% of cases. Young infants may continue to shed the virus up to 5 months after infection. The overall case-fatality rate is 0.3%, but it increases to 1.8% among persons aged ≥ 50 . Persons with underlying chronic liver diseases present an increased risk of death [40].

NV outbreaks cause acute onset of vomiting and diarrhoea affecting all age groups. Older references to NV infection as "winter vomiting disease" reflect that vomiting is often the first symptom. The predominance of vomiting is helpful for diagnosis. Fever occurs in one-third to one-half of patients; it is usually low grade and lasts for 24 hours. A variety of other symptoms including myalgia, headache and chills are also commonly reported. Symptoms generally last for 1-3 days [41]. Investigations of outbreaks of NV-associated gastroenteritis in the USA indicate that food was implicated in 37% of cases, person-to-person contact in 20% of cases, consumption of oysters in 10% of cases and water in 6% of cases [42].

HAV and NV are transmitted most commonly by contamination of uncooked foods by infected food handlers, but certain foods, such as bivalve mollusc shellfish and vegetables, may be faecally

contaminated at their source. Several studies have suggested that shellfish may play a significant role in the transmission of HAV. In Italy the data from SEIVA, a specific surveillance system of acute viral hepatitis, shows that the incidence of notified cases is declining. Nevertheless, at present, at least 1000 cases of hepatitis A per year are notified, 8% of which in 2001 and 2002 were associated with shellfish consumption [43].

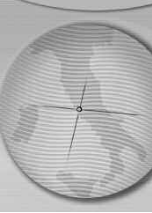
In Southern Italy, especially in Puglia, intermediate endemic levels of HAV still exist, in particular, in 1996 and 1997 two large outbreaks of hepatitis A occurred in Puglia, with 5673 and 5382 cases reported respectively. During 2004, a large outbreak of hepatitis A virus (HAV) occurred in Campania, once again in Southern Italy, with 882 cases reported from January 1st until August 1st. The epidemiological analytical study showed that raw seafood consumption, in particular those illegally kept in water, were strongly associated with the development of HAV illness [44]. The largest foodborne outbreak of HAV was reported in China in 1988, when over 300,000 people were infected after having eaten raw or improperly cooked clams [45].

Noroviruses are the most important cause of foodborne gastroenteritis in many developed countries, where they are estimated to account for more than two-thirds of the foodborne illness caused by known pathogens [2]. In The Netherlands, approximately 80% of gastroenteritis outbreaks reported to municipal health services are caused by NV [46].

In Italy, in July 2000, an outbreak of gastroenteritis occurred at a tourist resort in the Gulf of Taranto, in Southern Italy, with 344 cases reported. The source of the illness thought to be drinking water contaminated with norovirus [47].

NV have been associated with an international outbreak linked to oyster consumption involving a group of over 200 people in Italy and 127 total subjects in France. Almost four different strains of noroviruses were strictly correlated with the outbreaks; the multiple NV contamination was present in the oysters, and some strains were identical to the ones detected in French and/or Italian consumers [48].

The consumption of raw soft fruits and vegetables has recently been correlated with a large number of viral infections in various countries. Particularly, frozen raspberries have been linked to at least two outbreaks of hepatitis A virus [49, 50] and several outbreaks of noroviruses [51-54]. Outbreaks of HAV have been attributed to strawberries [55, 56], blueberries and lettuce [57]. Green onion was the cause of a wide



outbreak of HAV in the USA, involving approximately 555 persons, 3 of whom died [58].

Feline caliciviruses (FCV), used as a surrogate for enteric viruses like NV, show a great resistance to common disinfectants even when these are used at higher concentrations than those suggested by the manufacturers [59]. Prevention of viral enteric diseases depends on the elimination of faecal contamination of fruits, vegetables and water where shellfish are harvested. The improvement of food-handling practices, including the training of personnel and food handlers, is also important [60].

Conclusions

Despite the ever-increasing application of systems for process control and autocontrol, which are committed to ensuring the quality of food (Hazard Analysis Critical Control Point - HACCP in 1997, traceability in 2002, Good Agricultural Practice and HACCP in primary production in 2006), the emerging and re-emerging of biological, and especially microbiological, dangers continues to keep attention focused on the "risk" correlated with food consumption.

Foodborne diseases still represent an important public health issue all over the world, including in Europe and Italy, which endangers the health of the population and leads to socio-economic costs and a threat to the market trend.

In the European food production market, Italy (13.9%), France (18.4%), Germany (17.3%), UK (13.7%) and Spain (8.4%) are the largest EU-25 food and drink producers; together they account for more than 80% of the total EU production [61].

"Food safety" and, more generally, the "total quality of the supply chain", are one of the main purposes of EU policy which interacts with other policies such as: the Common Agricultural Policy (CAP), sustainable development and Public Health. Inspiring principles such as: a) the circulation of safe products for humans and animals; b) the guarantee of international relations; c) risk analysis based on scientific evidence.

The Regulation 178/2002/EC [62] has provided the most complete answer to the need for a food quality guarantee on a supranational scale, although the law revision process at Community level started with the Directives 89/397/CEE and 93/43/CEE [63, 64] and was completed when the regulations called the "Hygiene packet" came into force on the 1st January 2006 [65-68]. These regulations allow for the application of a unique and transparent Hygiene policy "from farm to table". They define clear responsibilities and provide efficient tools to ensure food safety and management of "emergencies";

among these tools are: the establishment of a European Food Safety Authority; the obligatory traceability of supply chains; risk analysis, which includes the scientific evaluation of known or potential adverse health effects (*Risk assessment*); the evaluation of the efficacy of different courses of preventive/corrective actions (*Risk management*) and the planning of actions to exchange information among all interested parties (*Risk communication*) in case of "emergencies".

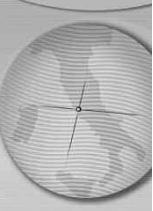
Communication as well as educational campaigns aimed at different target groups such as consumers, parents, children, people who work in professional kitchens or prepare food at home, street food vendors etc., will play an important role in the prevention of foodborne diseases. In this respect, the WHO has developed a simple claim based around the "written common sense" = "Five Keys to safer food": keep clean; separate raw and cooked; cook food thoroughly; keep food at safe temperature; use safe water and raw materials [69].

Responsibility for safe food production is now defined and is shared between operators, National Authorities and the European Commission. Operators are responsible for compliance with legislative provisions and for minimizing risk by their own initiatives, while National Authorities are responsible for ensuring food safety standards are respected by the operators. However, they need to establish control systems to ensure that Community rules are being respected and, where necessary, enforced.

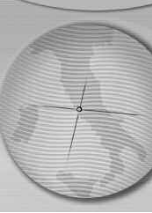
These systems need to be developed at the Community level, so that a harmonized approach can be followed.

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